Cavitands, Liquid Crystals and Antibodies: Materials for Integrated Chem/Bio. Sensing

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Outline

- Technology Gaps
- Goal, approach
- Cavitands for chemical vapor sensing
- Liquid Crystals for sensitivity amplification
- Label-free antibodies for SPR biosensing
- Conclusions

Technology Gaps

- Chemical detectors
  - limited sensitivity - still use canines for bomb detection
  - high false alarm rates – limited specificity
  - slow response time – due to sensing material used
- Biological Detectors
  - need reagents, labels, not real time
- Separate Detectors
  - for chem. and bio. threats increase logistical burden/cost

Goal

Develop an integrated SPR chem/bio detector with

False Alarm Rate < 10^{-3} for chem. and < 10^{-8} for bio.

Sensitivity – below permissible exposure level (PEL) for chem.

- LOD of 100 organisms/liter of air for bacteria/viruses
- LOD of 10 nanograms/liter of air for toxins

Response time - < 1 minute for chem. and < 10 min for bio.

Military and civilian need

Chem/Bio detectors with high sensitivity, specificity, stability, and speed in portable format for airborne threats

Approach

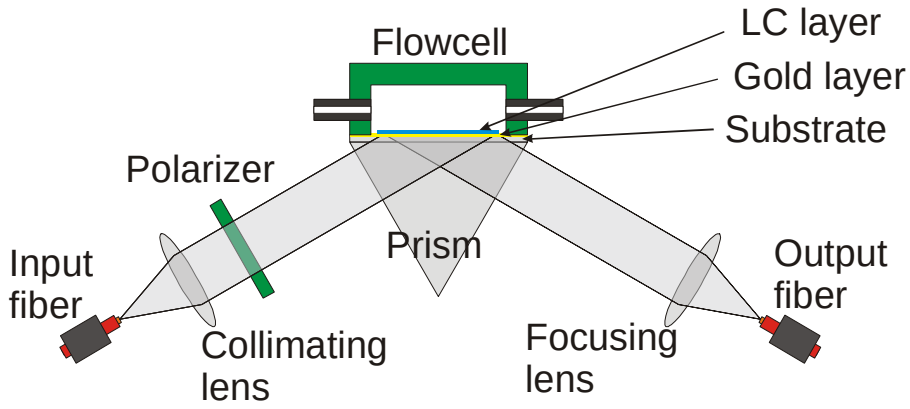
Technique - SPR spectroscopy

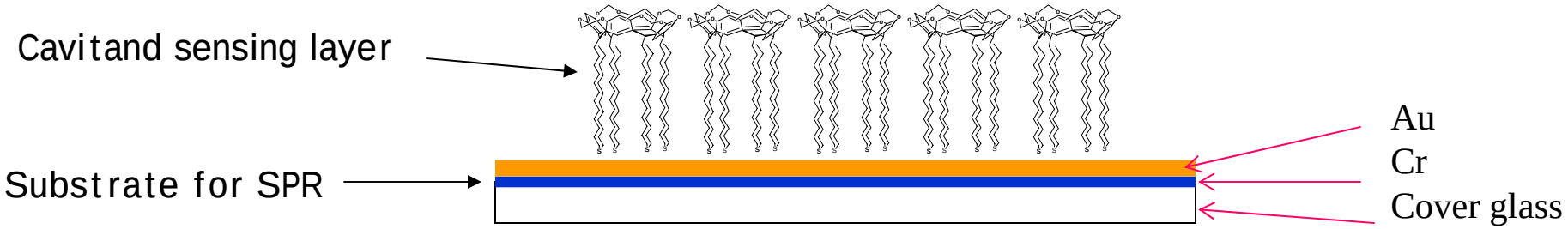
Sensing with - Cavitands for chem. threats

- Liquid Crystals for chem. threats

- Antibodies for bio. threats

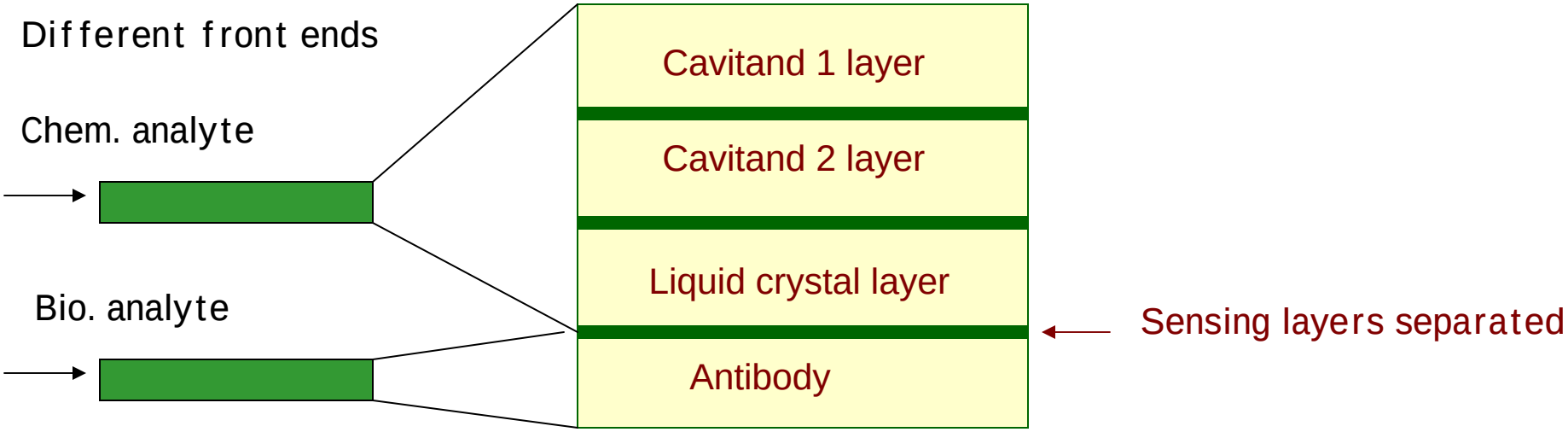
- Sensitive optical transduction technique – part in 10^7 refractive index changes can be measured





Integration of chem/bio.

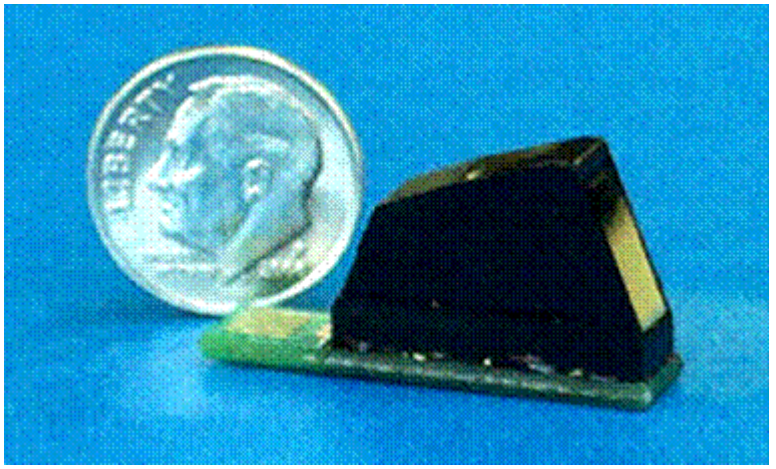
- Common optical and data processing platform
- Different front ends for chem. and bio. samples
- Isolated channels for chem. and bio. sensing layers



Top View of SPR substrate

Sensor Components:
TI Spreeta 2000 (3-channel)

- Spreeta 2000 SPR components developed in collaboration with UW
- Miniaturized, robust, high performance devices
- Inexpensive: ~$4 in large quantity
- Excellent manufacturing capabilities and quality control.



Spreeta 2000 SPR sensing chip

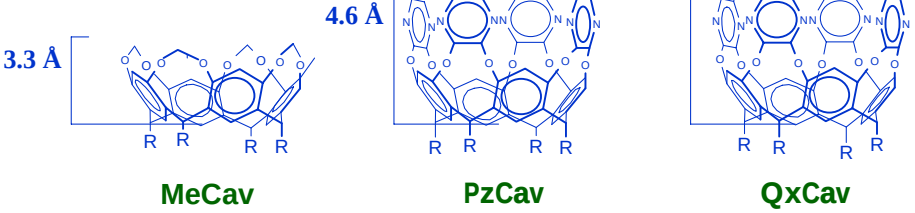
CBW Agents Detectable with SPR

Type of Agent	Examples of Agents of Interest	Current Direct Detection level	Amplification/ verification
Protein toxins	SEB Ricin Botulinum toxin,	100 pM (2.8 ppb) 20 nM (64 ppb; current level) <50 nM (750 ppb, current level)	Yes (2.8ppt) Not yet done Yes
Spores	*B. Anthracis,* BG spores *(simulant)*	~10^5 cfu/ml (prelim)	Not yet done
Viruses	Small pox, Marburg, Ebola, Encephalitis, Hemorrhagic fever Flu (as a model system)	~10^9 pfu (prelim expts)	Yes (prelim)
Microbial cells	*Y. pestis* *F. tularensis* *E. Coli*	In progress ~5x10^4 cfu/ml (prelim) In progress	Yes Not yet done Yes
CW (organics)	VX Soman Sarin tabun *DPMP(stimulant* Domoate Cortisol DNP	Antibodies tested at ECBC 50 nM (15 ppb) 750 pM (271 ppt) ~1 uM (340 ppb)	

C. Furlong et al, U. Washington

Cavitand Selectivity

Feresenbet, E.; Dalcanale, E.; Dulcey, C.; Shenoy, D.K.,
***Sensors and Actuators B*, 97, 211 (2003)**



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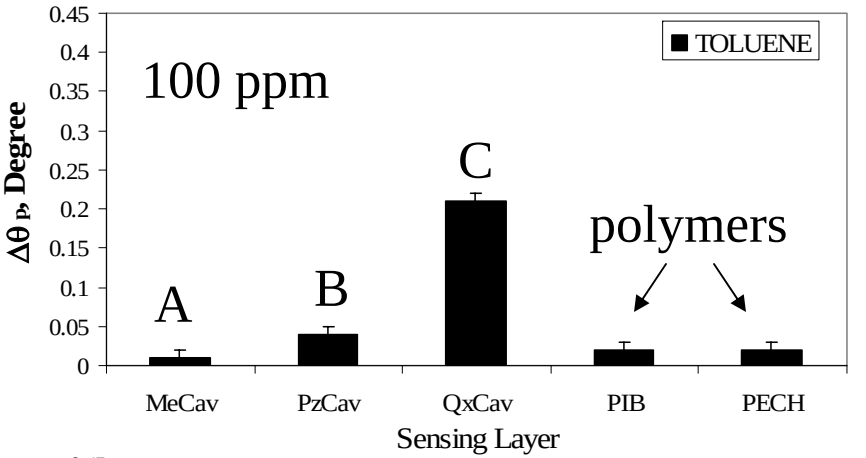
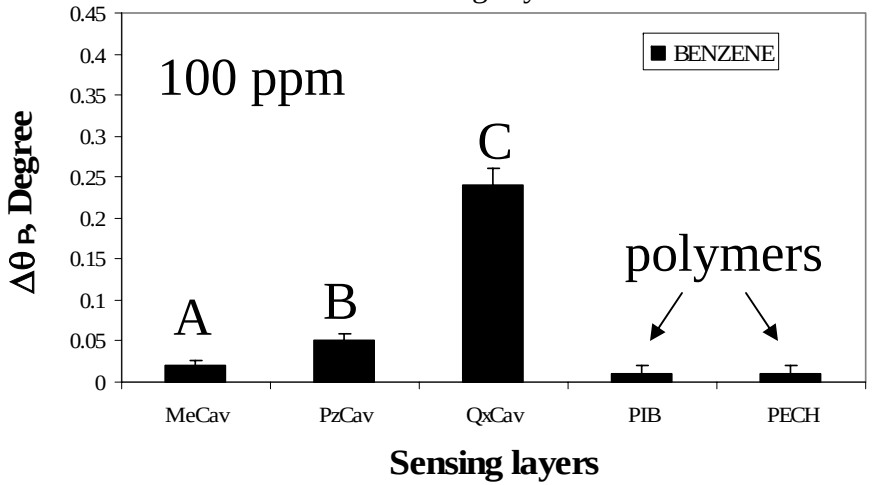
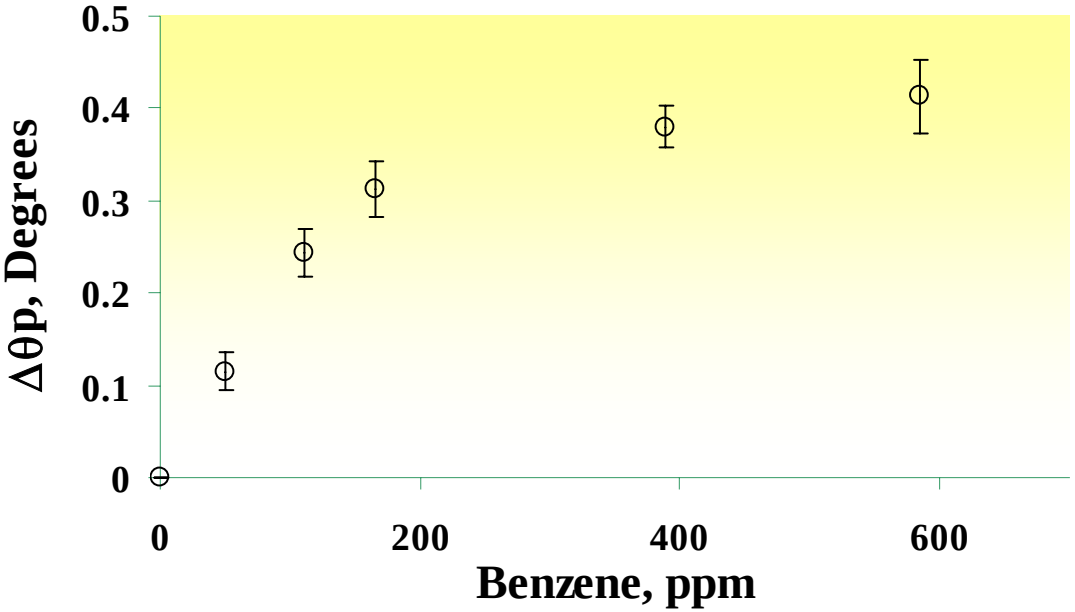
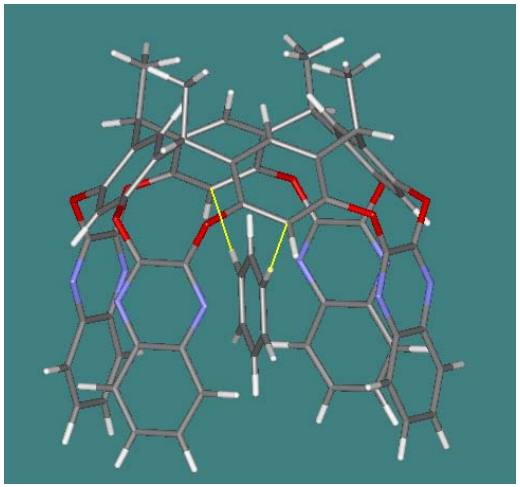




- Cavitand with deepest cavity shows largest response
- Selectivity for aromatic vapors confirmed
- PECH and PIB polymers for comparison

Concentration Dependence of Signal



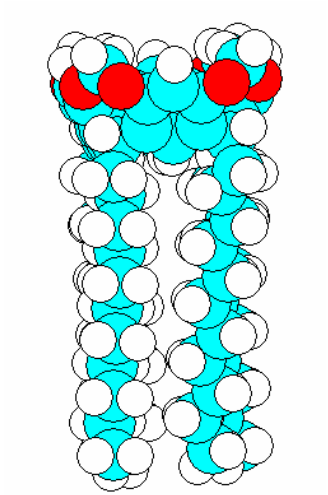


QxCav-Benzene complex

- Saturation due to analyte "filling" of cavitands
- QxCav completely encloses benzene molecule within cavity

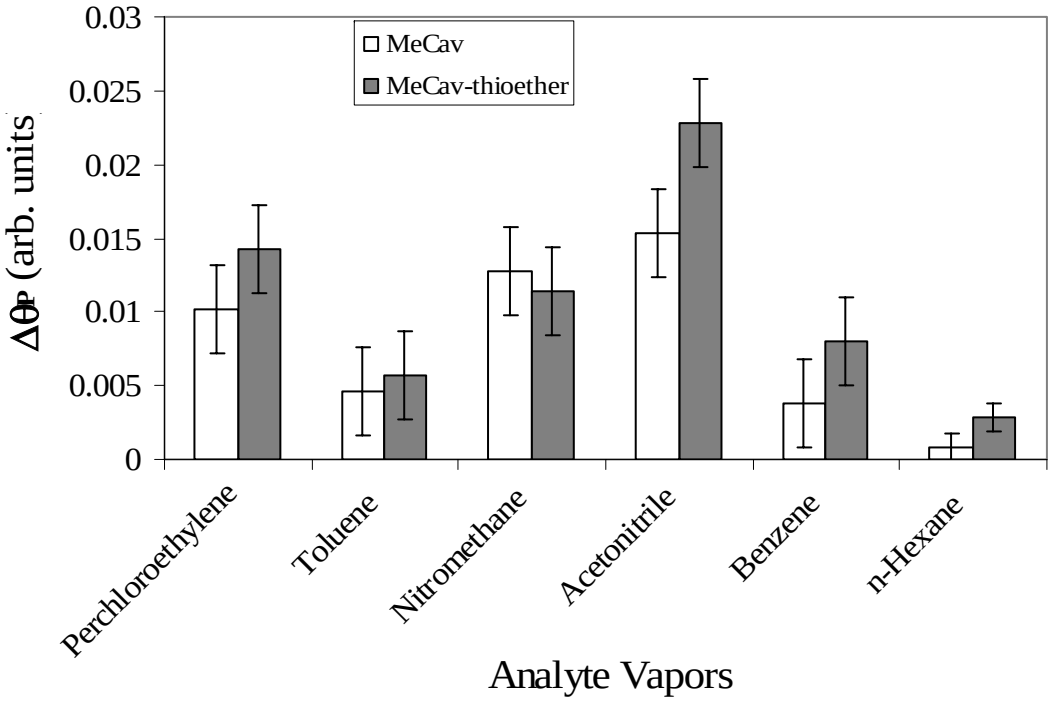
Materials Processing:
Spin Coated vs Self-Assembled Cavitands

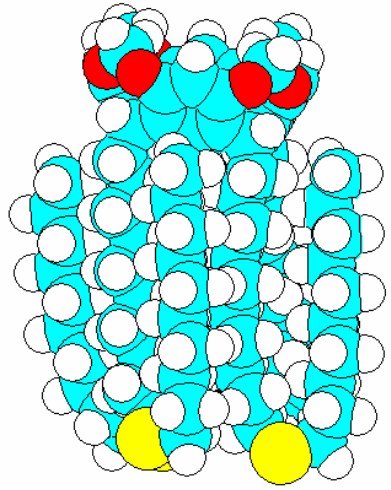
Devanand K. Shenoy, Elias B. Feresenbet, Roberta Pinalli, Enrico Dalcanale;
Langmuir 2003, 19, 10454



MeCav

Spin coated



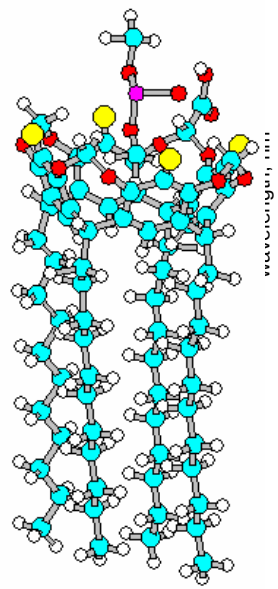


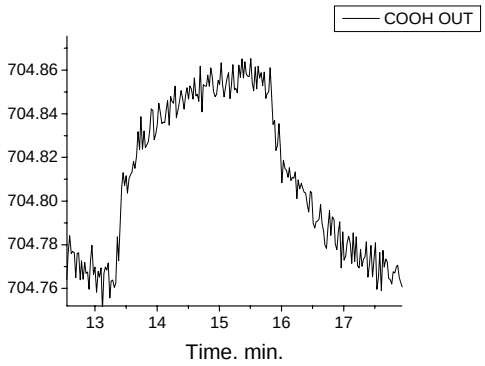
MeCav-thioether

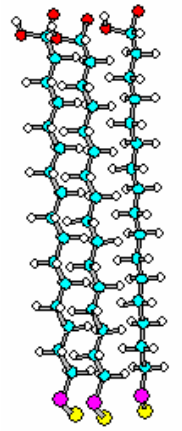
Self-assembled

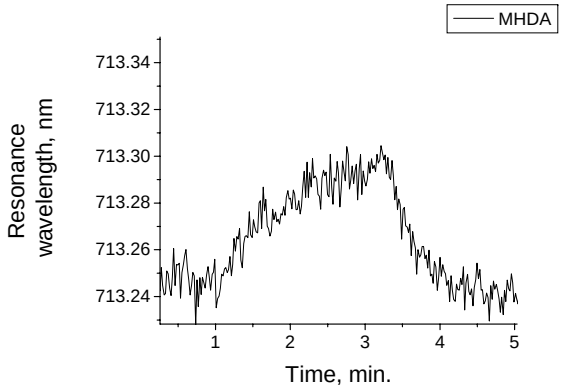
- Cavitand Morphology does not effect signal response
- Signal response normalized for thickness

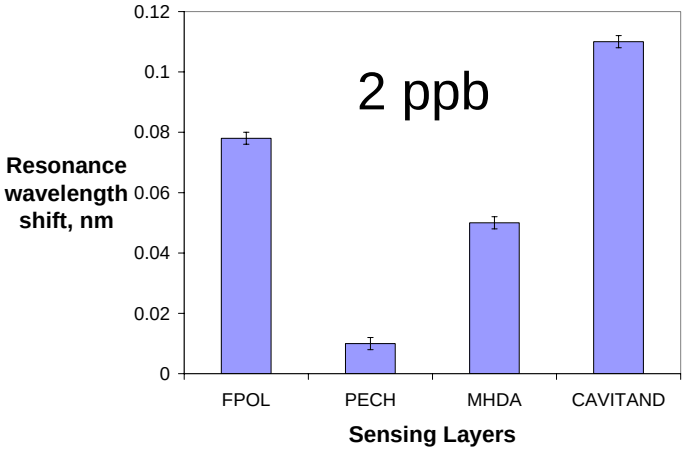
Cavitands for DMMP

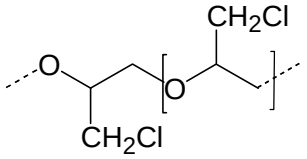


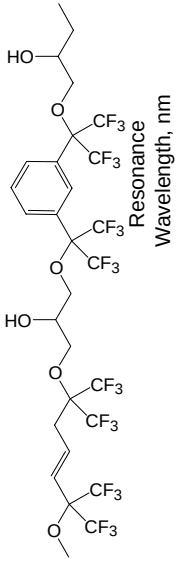


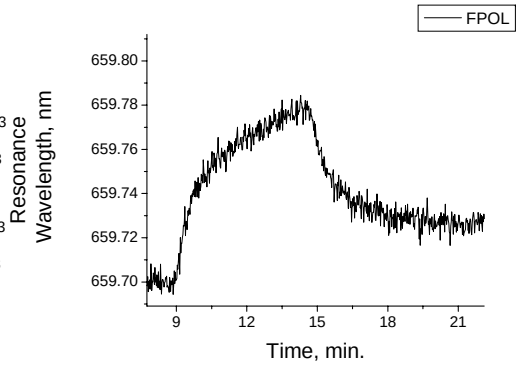


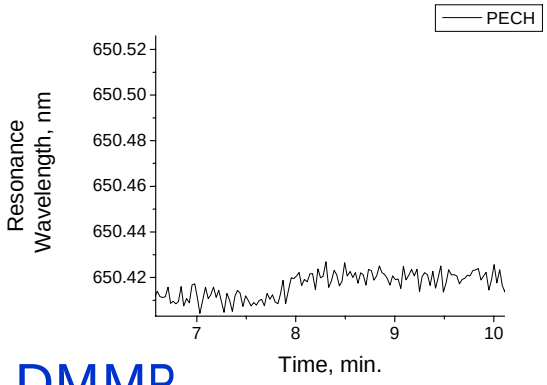








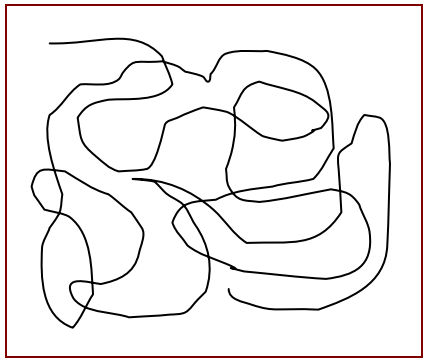


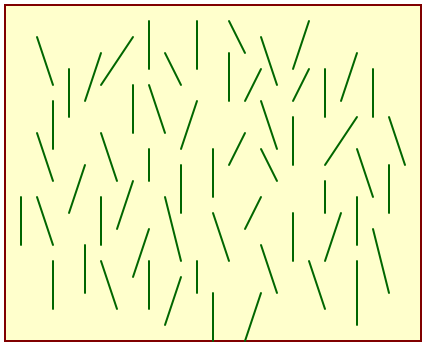


- Cavitand shows high selectivity for DMMP
- Cavitand shows good reversibility

Liquid Crystal-based Sensing

Polymer
Sensing layer

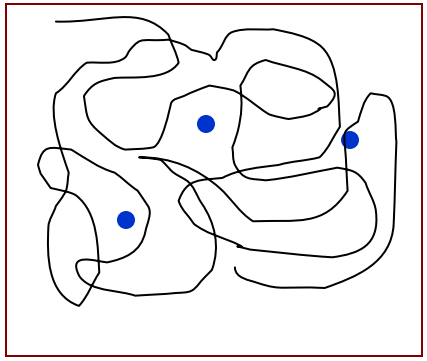


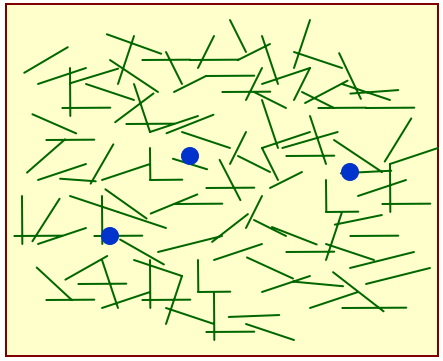


Liquid Crystal
Sensing layer

● **Analyte**

Local perturbation

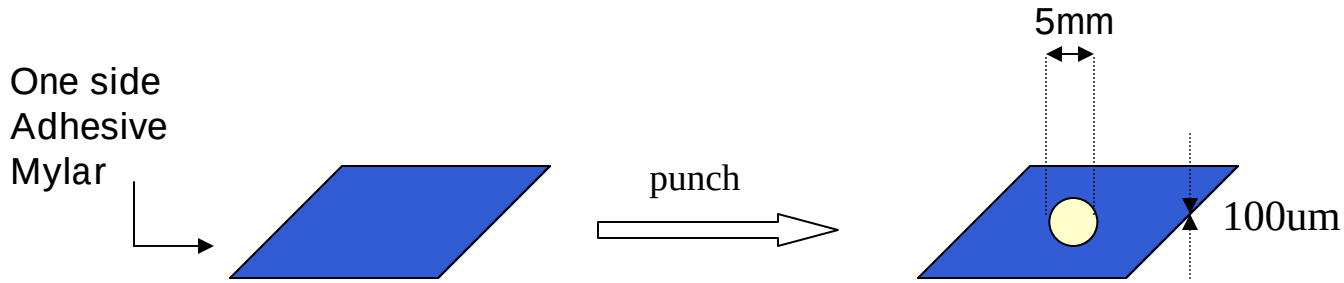


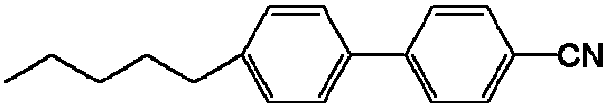


Global perturbation

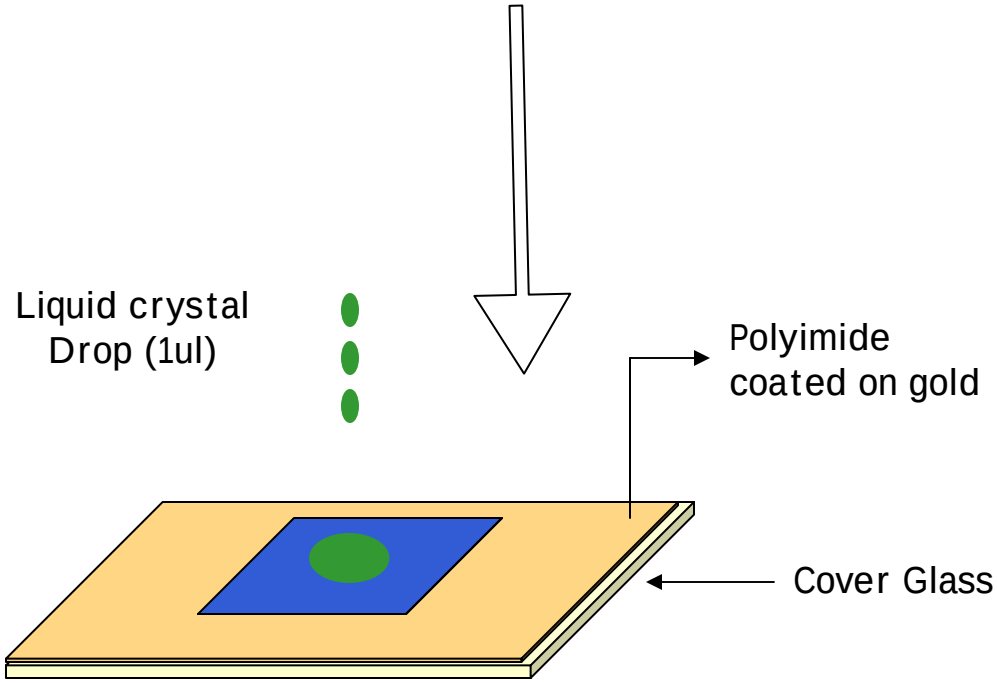
- Liquid Crystal (LC) perturbation causes **signal amplification**
- **Nematic order** probed by optical method
- Optical signal directly proportional to amount of vapor

LC film deposition

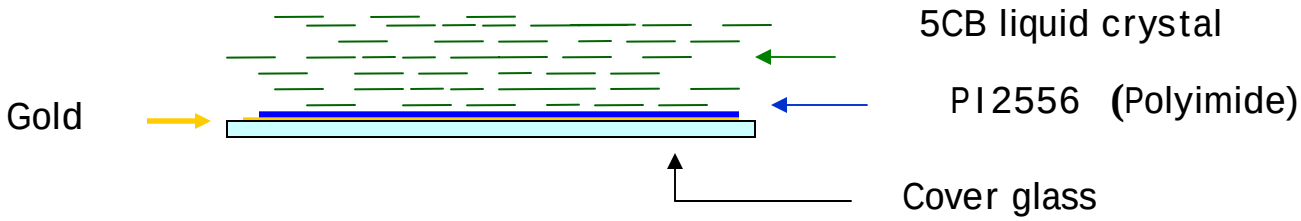


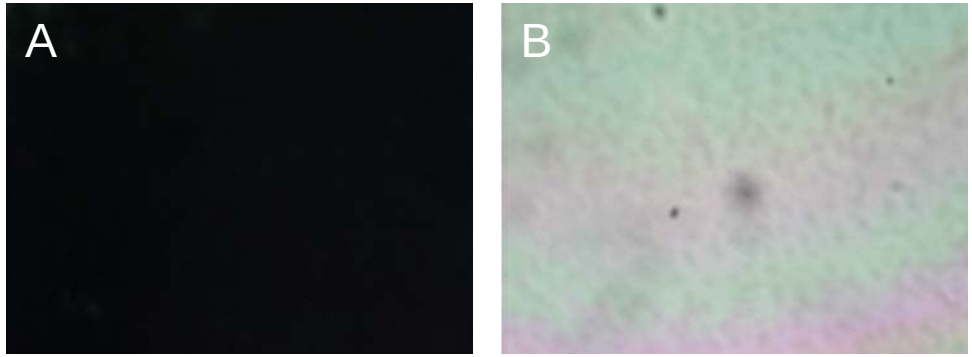


Liquid crystal molecule



LC alignment

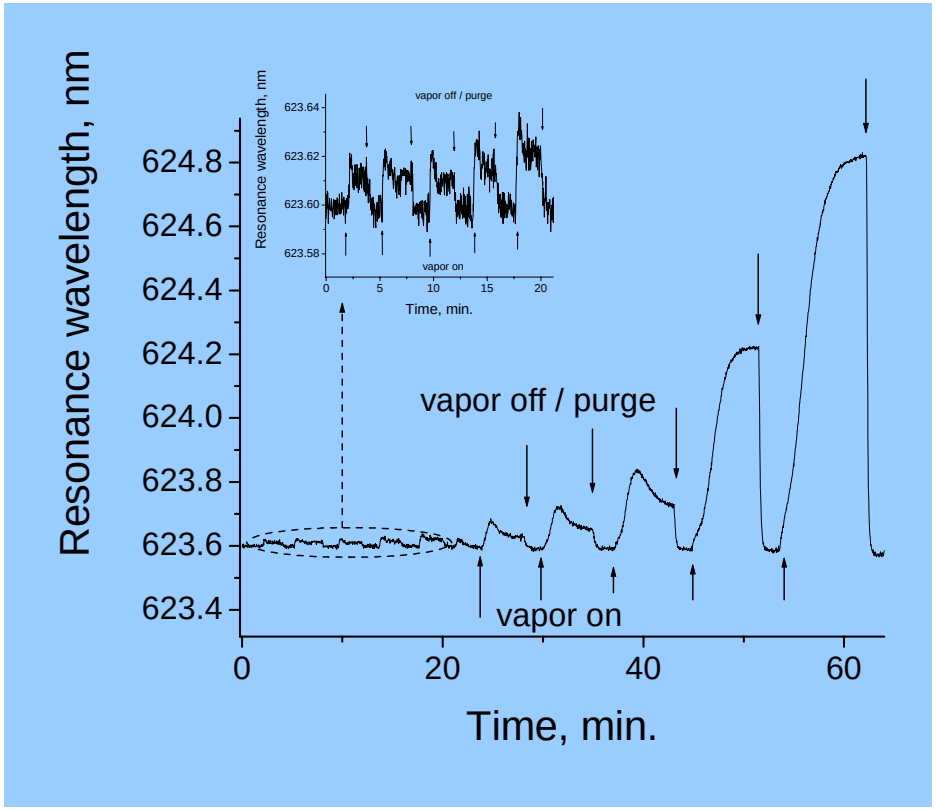


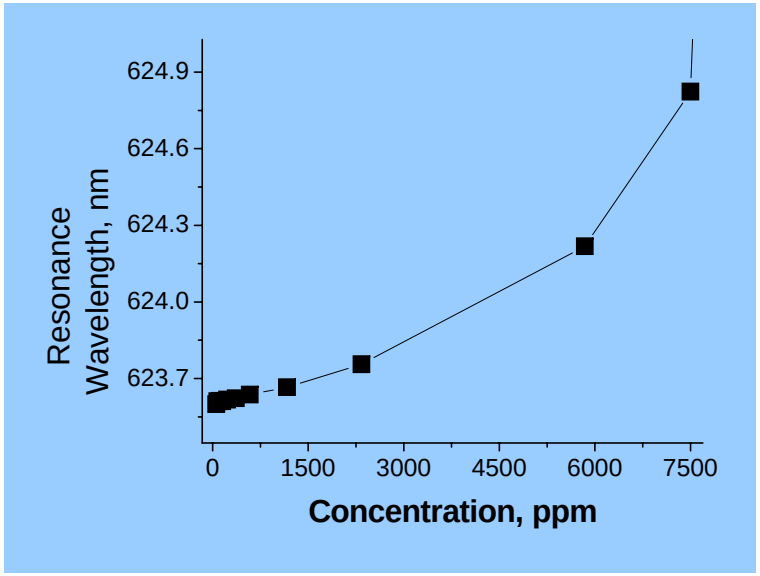


- A uniform planar orientation achieved

LC exposure to benzene vapors

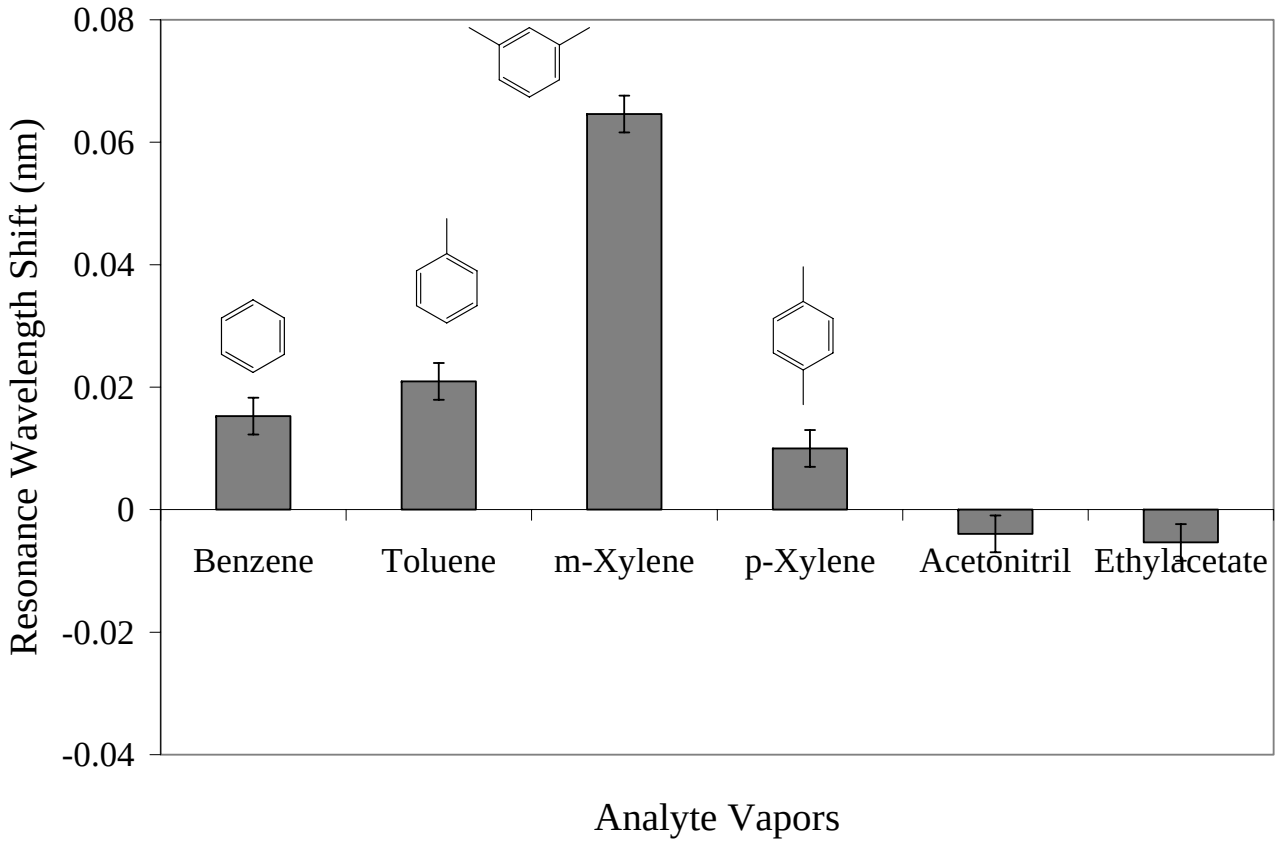
E. Feresenbet, F. Taylor, T. M. Chinowsky. S. S. Yee, D.K Shenoy, Sensor Letters 2, 145-152, 2004





- Wavelength shift due to vapor exposure and resulting decrease in LC order
- Shift is reversible

Selectivity pattern of LC towards vapors

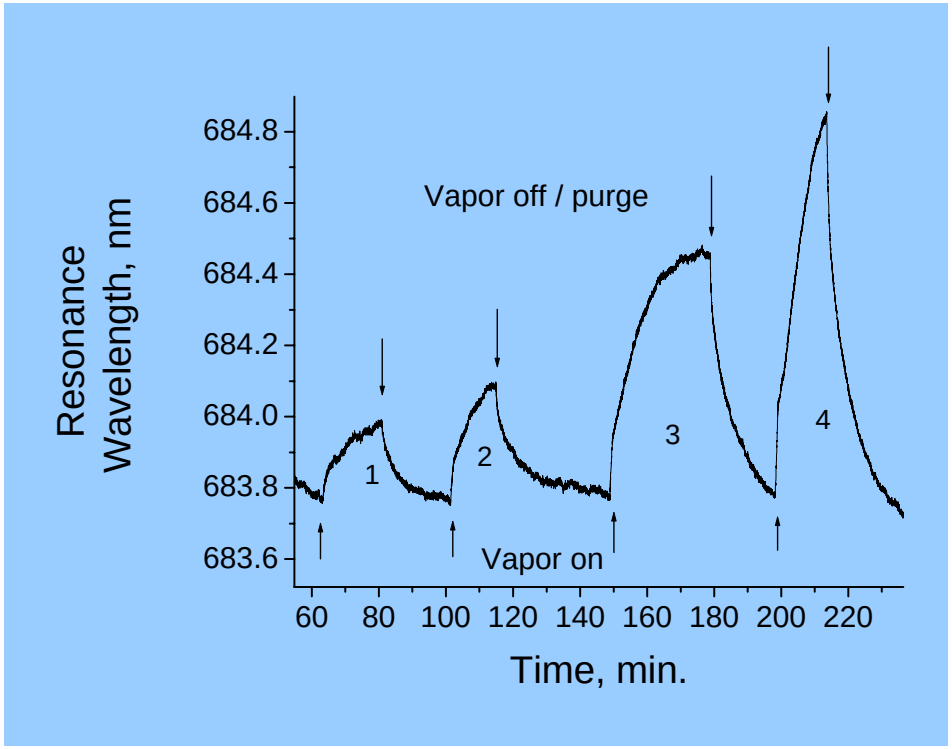


- LC shows differential response to chemical vapors
- Selectivity between isomers observed

LC exposure closer to phase transition

nematic ⟷ isotropic

35.1°c

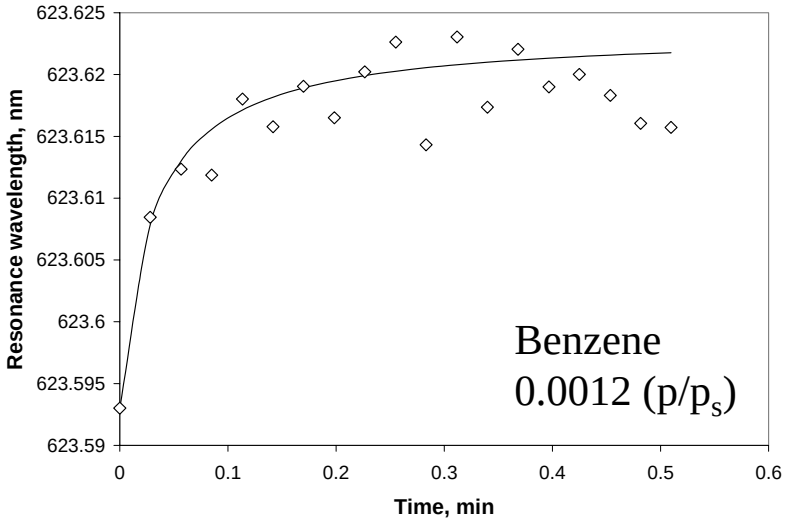


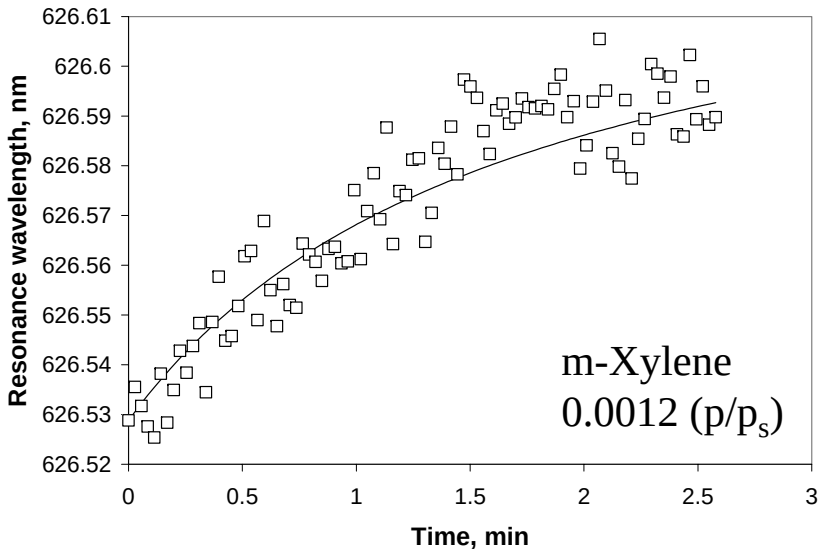
m-xylene

	ppb
1	270
2	380
3	680
4	850

- Sensivity enhanced by two orders closer to phase transition
- Shift is reversible

Kinetics of Response





$d\lambda/dt = k\lambda^2$

λ = resonance wavelength (nm)

t = time (min)

k = rate constant

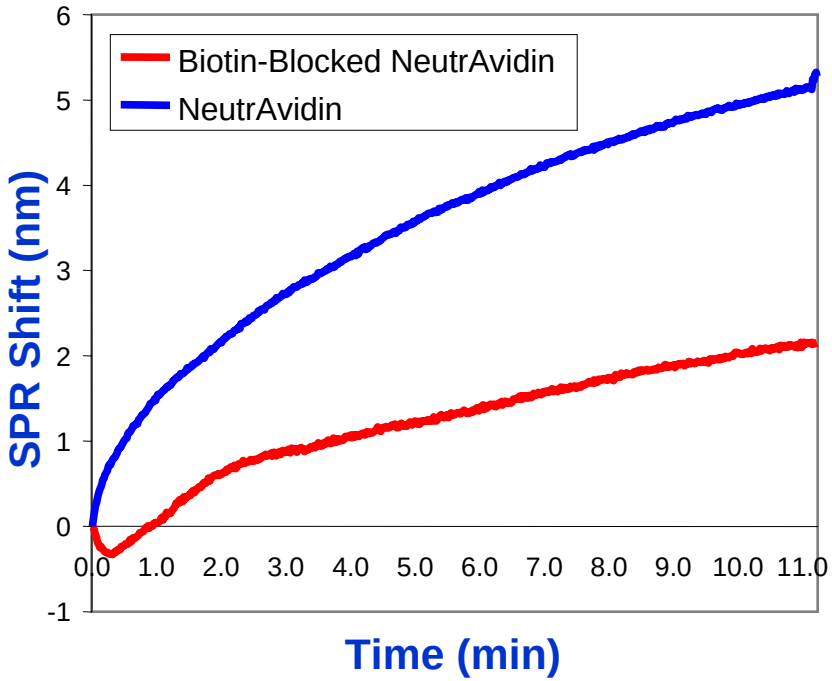
- Second order kinetics describes data for vapor diffusion into LC
- Time response additional selectivity parameter

E. B. Feresenbet, F. Taylor, T. M. Chinowsky, S. S. Yee, and D. K. Shenoy, Sensor Letters, 2, 145-152, 2004

SPR Biosensing

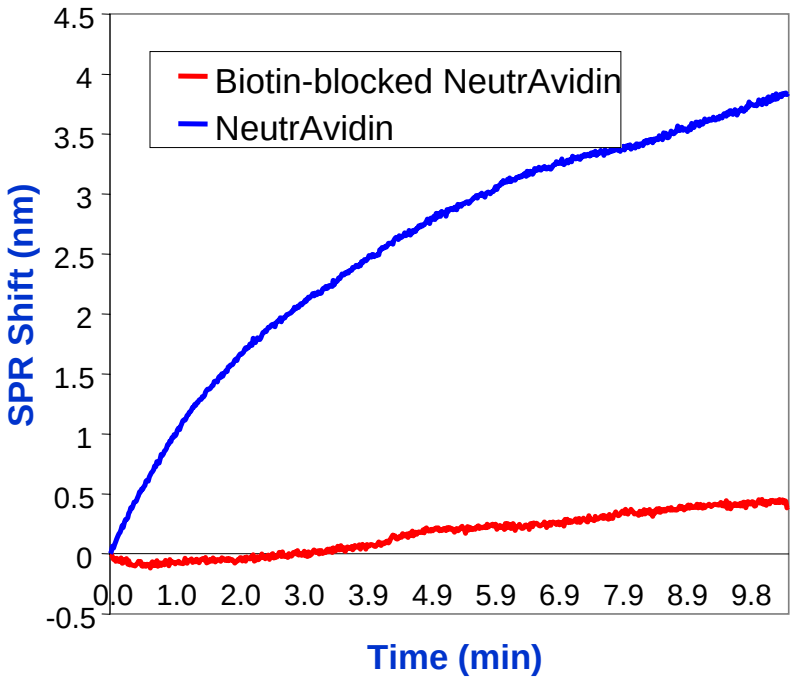
- Neutravidin-Biotin mediated antibody immobilization

➢ Effect of blocking binding to thiol-biotin coated gold surface



➢ NeutrAvidin blocked by biotin binds poorly to the thiol biotin surface

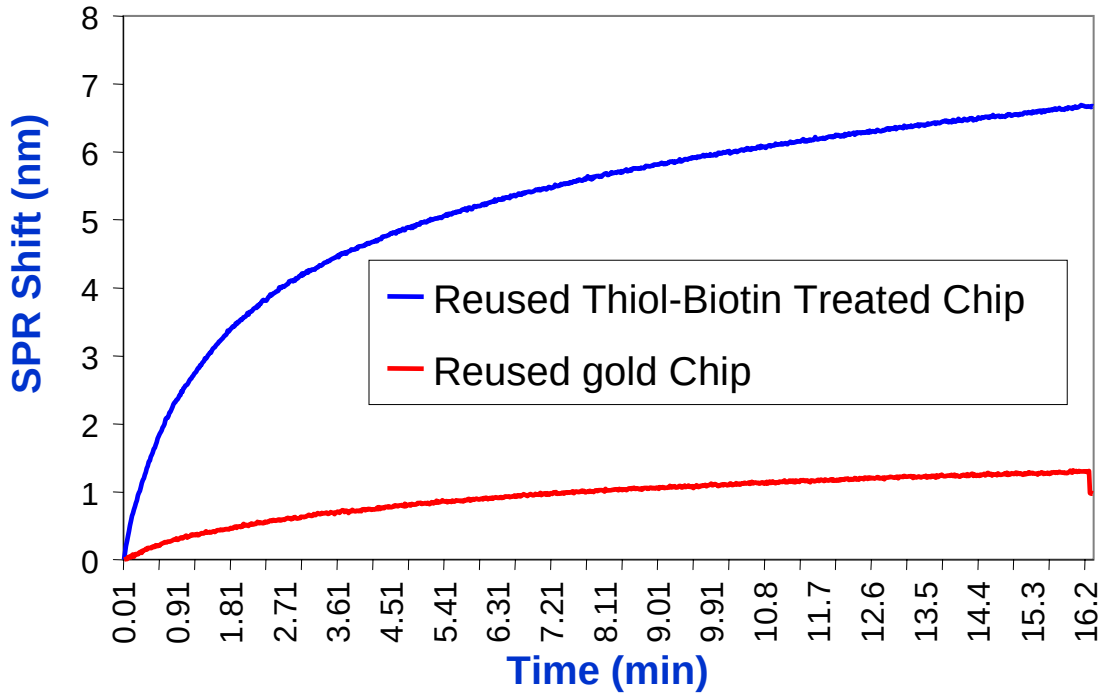
➢ Effect on binding of biotinylated antibody



➢ Subsequent binding of the biotinylated antibody is also poor

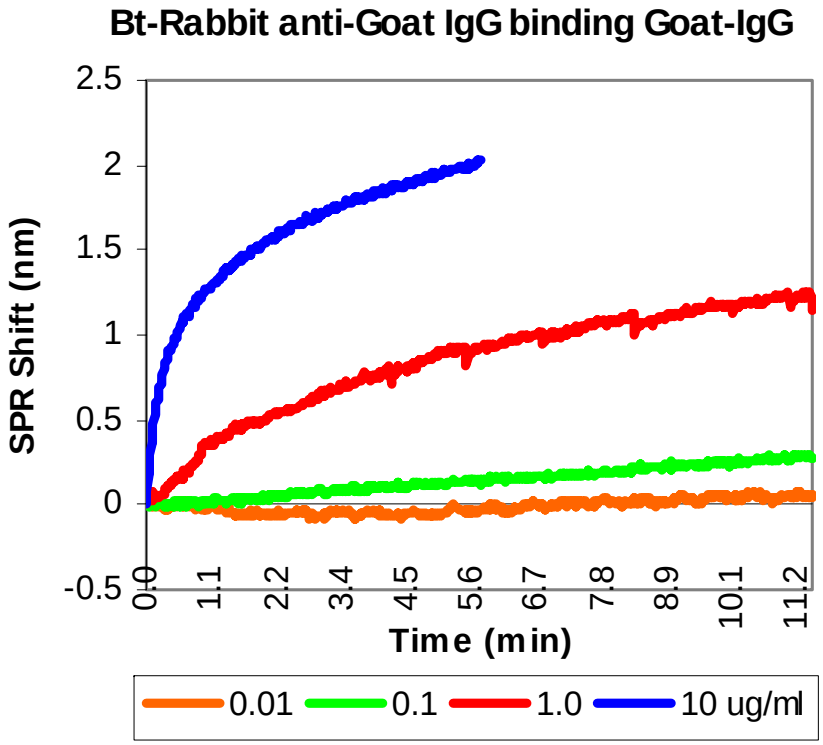
Re-cycling the sensor surface

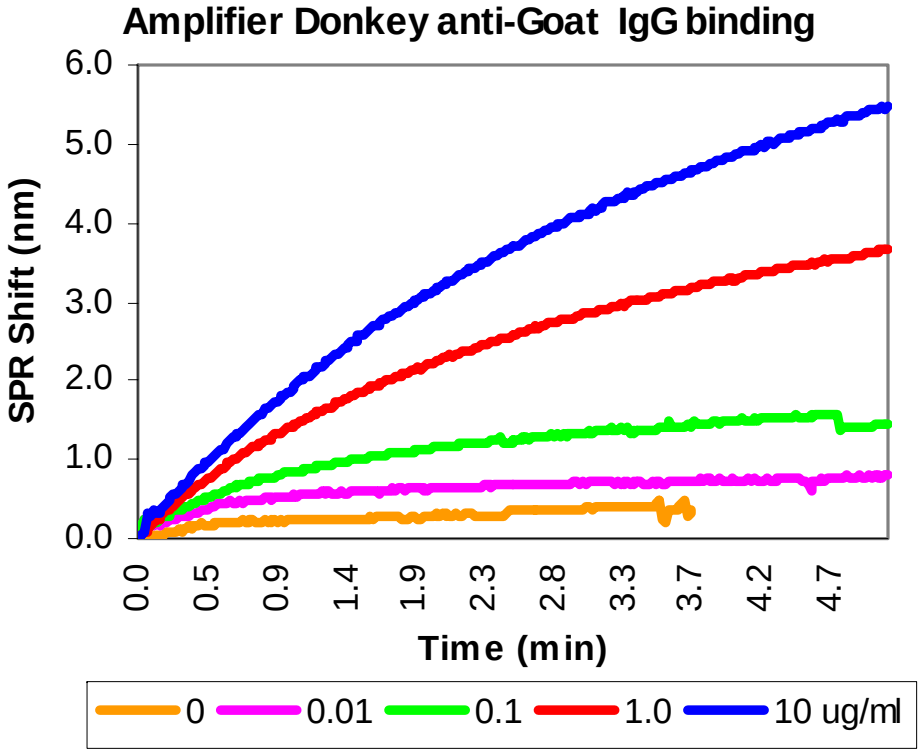
- Neutravidin binding to different sensor surfaces



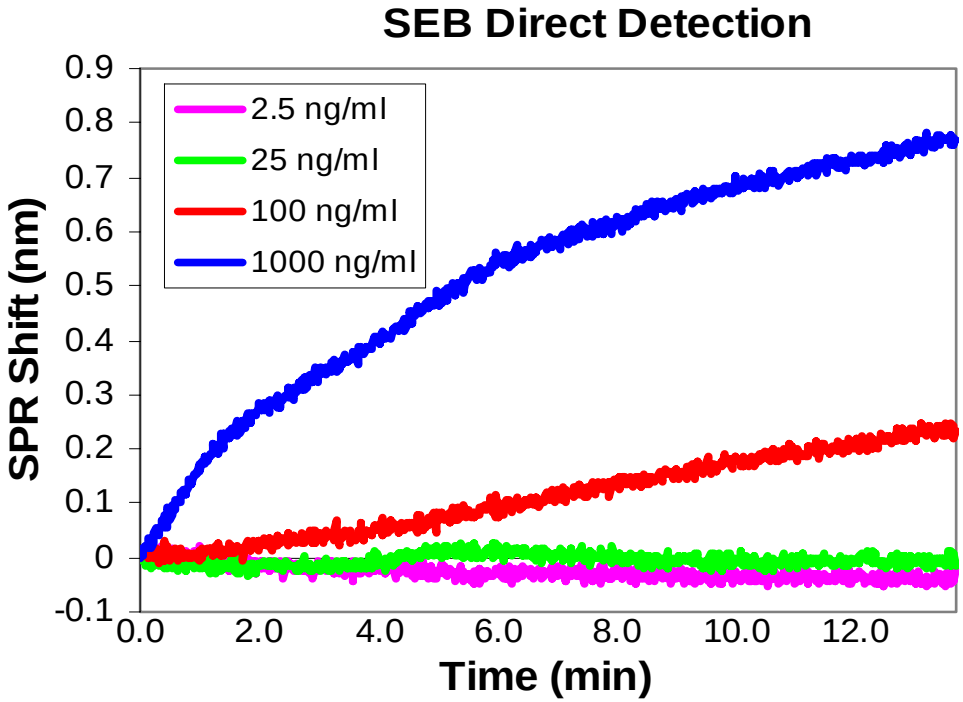
- Neutravidin binds as well after cleaning of the gold surface and re-application of the thiol biotin layer

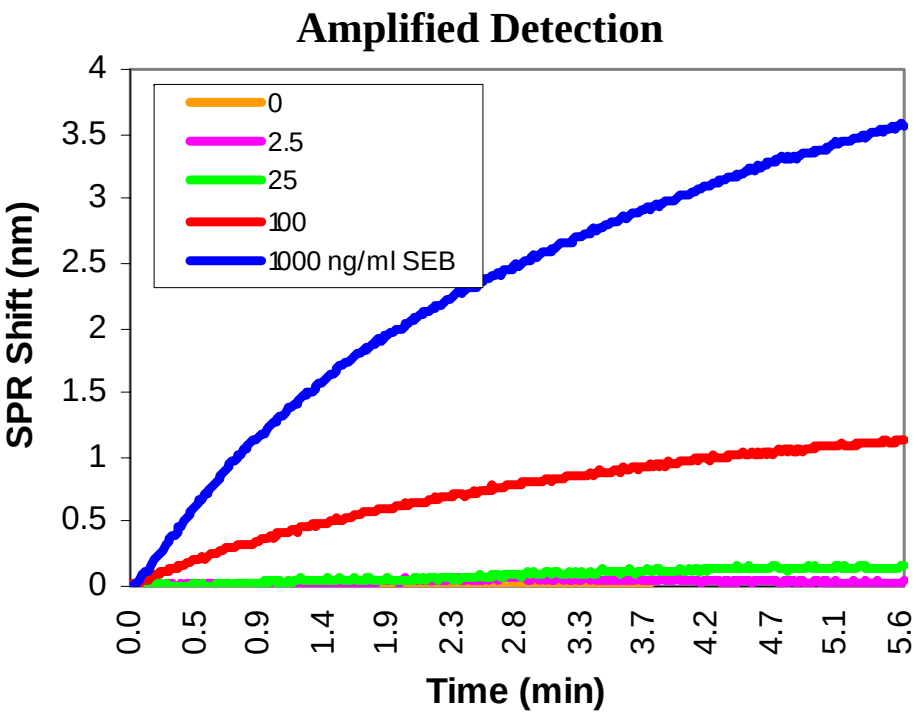
SPR model immunoassay

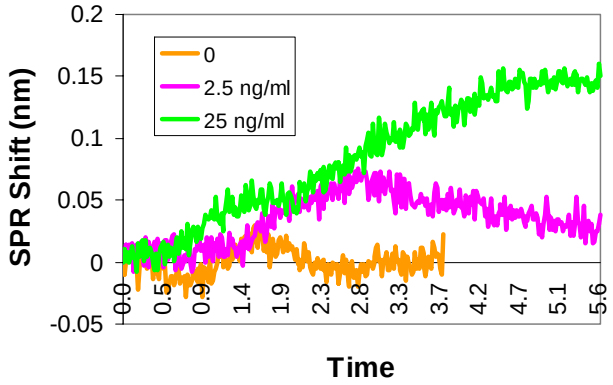




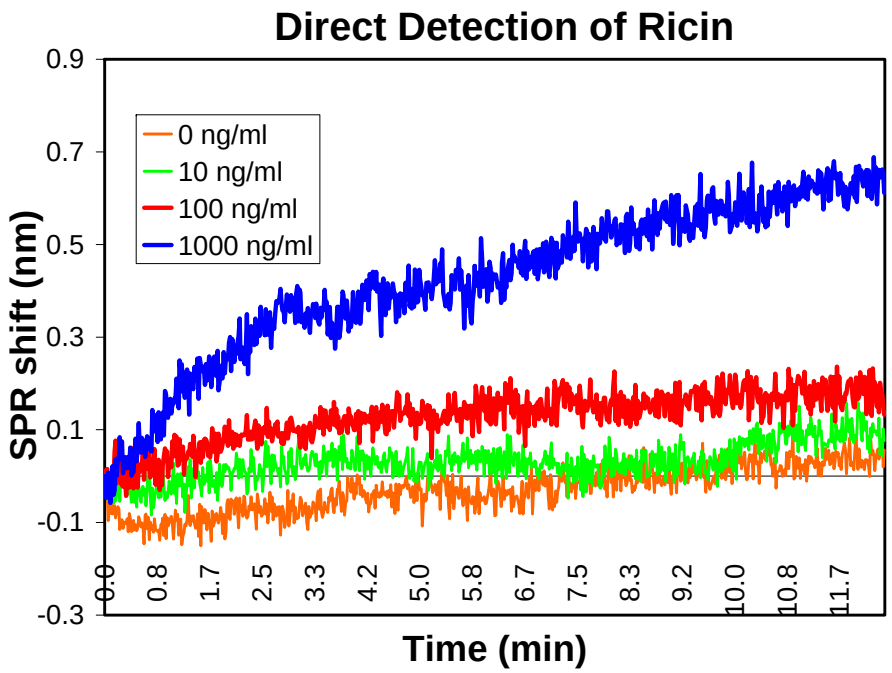
Staphylococcal Enterotoxin B detection by SPR

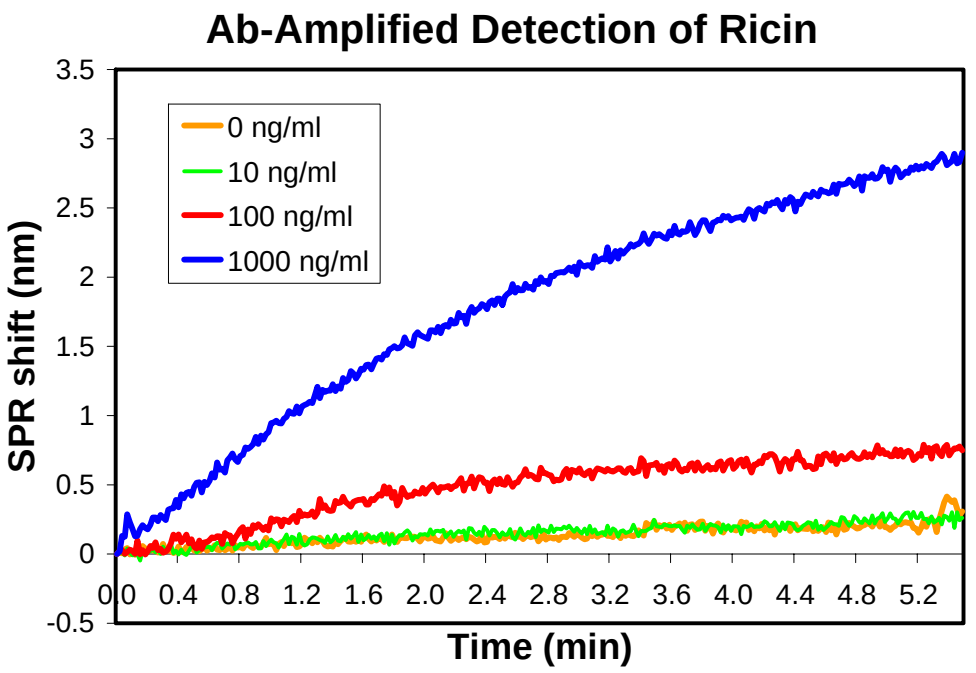




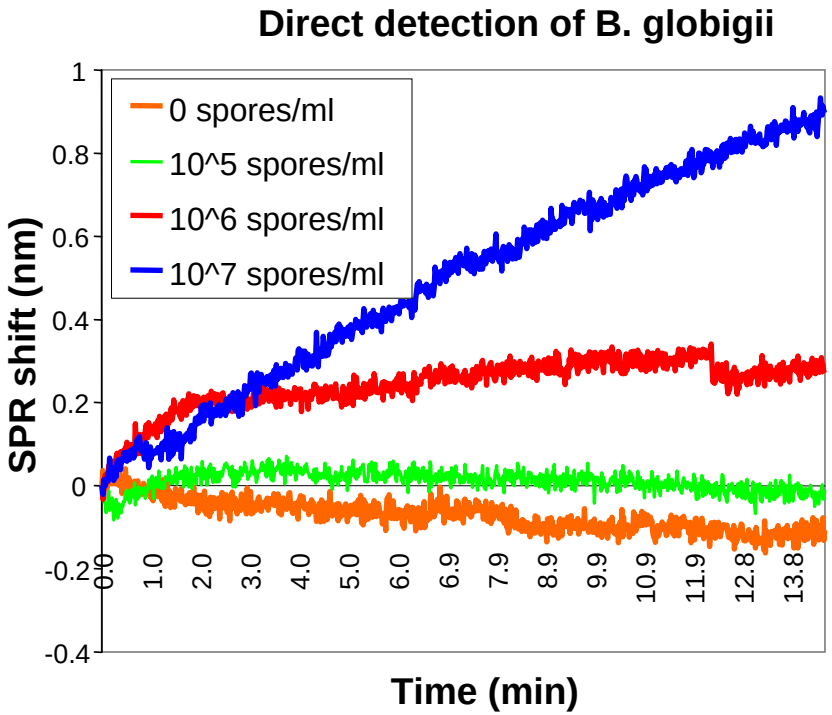


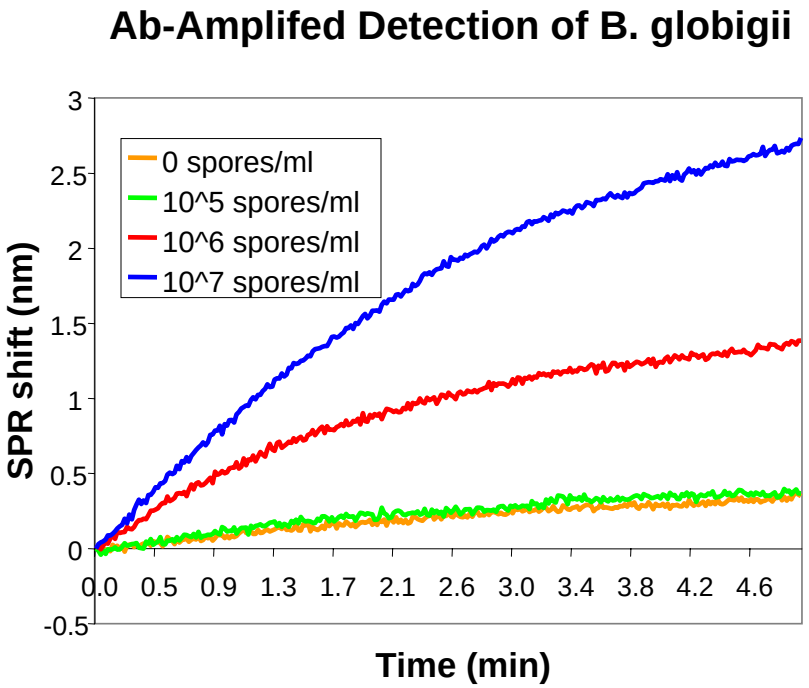
Ricin detection by SPR





Bacterial spore detection by SPR





Conclusions

- ✓ Cavitands show high selectivity for chemical vapors
- ✓ Cavitand film morphology does not affect signal response
- ✓ Liquid Crystal materials for sensitivity amplification
- ✓ Label-free, real-time SPR biosensing
- ✓ Integration of chem. and bio. approaches appears feasible

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